47.(New) The method of claim 43, wherein the anemia is associated with renal transplantation.

48. (New) The method of claim 43, wherein the anemia is associated with cancer.

49.(New) The method of claim 43, wherein the anemia is associated with acquired immune deficiency syndrome.

50.(New) The method of claim 43, wherein the anemia is associated with chemotherapy.

51.(New) The method of claim 43, wherein the anemia is associated with radiotherapy.

52.(New) The method of claim 43, wherein the anemia is associated with bone marrow transplantation.

SUPPORT FOR AMENDMENTS

New claims 45-52 are supported by claim 43 as originally filed. Other amendments merely clarify the claims, and do not introduce new matter.

REMARKS

Election/Restriction

Pursuant to the telephone conversation with the Examiner on February 25, 2002, the Applicants hereby affirm with traverse the election of species corresponding to SEQ ID No.9.

The Examiner withdrew claims 34-37 and 39 from further consideration. The Applicants traverse the decision to withdraw claims 35-37 on the ground that claims 35-37 are readable upon the elected species of SEQ ID No.9. Claims 35, 36 and 37 recite the method of claim 1 wherein the active agent consists essentially of a sequence of at

least three, four, or five contiguous amino acids, respectively, of groups R1-R8 in the sequence of general formula I. SEQ ID No:9 consists of five amino acids, and is therefore encompassed by claims 35-37, which are therefore **not** drawn to a non-elected invention. The Applicants therefore respectfully request that claims 35-37 be reinstated and considered by the Examiner.

Claim Rejections Under 35 USC §112

4. The Examiner rejected claims 1-2, 31-33, 38 and 40-44 as being indefinite under 35 U.S.C. §112, second paragraph, based on the assertion that the claims are indefinite for, (a) not indicating when to stop the contacting of the active agent, and (b) the use of "between" and "about".

The Applicants traverse the rejection, but have nonetheless amended the claims to obviate the rejection. Accordingly, the Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections Under 35 USC §103(a)

5. The Examiner rejected claims 1-2, 31-33, 38 and 40-44 under 35 U.S.C.§103(a) as being unpatentable over Mrug et al. in view of Pfeilschifter et al.

The Examiner asserted that it would be obvious to one of skill in the art to use AII(1-6) to augment erythropoiesis in view of Mrug et al., which is asserted to teach AII stimulation of erythropoiesis via the AT1 receptor, and Pfeilschifter et al., which is asserted to teach that AII(1-6) shows some affinity for the AT1 receptor. The Applicants traverse the rejection.

The Applicants respectfully note that the peptide Asp-Arg-Val-Tyr-Val-His, which is referred to as AII(1-6) by the Examiner and is asserted by the Examiner to be taught by Pfeilschifter et al., does not correspond to any of the sequence in the Sequence

Listing submitted with the application. The peptide sequence of AII(1-6) is Asp-Arg-Val-Tyr-Ile-His, corresponding to SEQ ID No:8.

One of skill in the art would not find that the combination of Mrug and Pfeilshifter makes it obvious that AII(1-6) would stimulate erythropoiesis for the following reasons:

(1) Pfeilshifter teaches nothing at all about any effect of any compound on erythropoiesis.

(2) It is known in the art that AII(1-7) does not act via the AT1 receptor. Ferrario et al. (Ferrario, C.M., et al. *J. Am. Soc. Nephrol.*, 9:1716-1722 (1998)) state explicitly that "..the majority of the data available currently suggest that Ang-(1-7) may act at a novel non-AT1/AT2 receptor subtype, the signal transduction pathway for which still remains to be elucidated." (page 1718, left col. 48-51) The Applicants hereby respectfully submit the above-mentioned reference for the Examiner's review.

(3) Pfeilschifter et al. demonstrate that AII(1-6) and AII(1-7) have some effect on choline formation in mesangial cells, but the effect is much weaker than that of AII. In fact, the effect of AII(1-6) shown in figure 4 is virtually identical to that of AII(1-7) or control, which is significantly weaker than that of AII.

(4) Pfeilschifter et al. demonstrate that the AII effect is mediated via the AT1 receptor. The inhibitory effect of AT1 receptor antagonist DuP753 on choline formation was only shown with respect to AII (figure 5), therefore Pfeilschifter et al. do not demonstrate, nor do they suggest that the weak effects of AII(1-6) or AII(1-7) are mediated via the AT1 receptor.

Based on a combination of the above-mentioned points that (A) the effect of AII(1-7) is not mediated via the AT1 receptor; (B) the effect of AII(1-6) on choline formation resembles that of AII(1-7); and (C) Pfeilschifter et al. do not show any data that the effect of AII(1-6) is mediated via the AT1 receptor, one of skill in the art would not find it obvious that AII(1-6) would have similar effects to AII in mesangial cells, and would in fact believe that AII(1-6) does not activate choline formation via the AT1

receptor, similarly to AII(1-7). In fact, the passages of Pfeilschifter et al. imply that AII(1-7) and AII(1-6) do not act via the AT1 receptor. On page 60, right col., lines 1-6 it states: "Figure 4 demonstrates that angiotensin II is a potent stimulator of [^{3}H] choline formation in mesangial cells. In contrast, angiotensin (1-7) and angiotensin(1-6) have only weak effects. These findings suggest that the angiotensin II AT1 receptor may mediate phospholipase D activation." This statement clearly implies that the effects of AII, AII(1-6) and AII(1-7) are mediated via different receptors. Similar statements could be found in the Abstract (lines 8-10), and Discussion (page 61, left col. lines 4-10 under Discussion).

Furthermore, one of skill in the art would certainly not find that the cited references make it obvious that AII would have the same effect on erythropoiesis as AII, since the AII and AII(1-6) effects were significantly different in mesangial cells.

The Examiner further asserts that "for the treatment of anemia, such language is an intended use limitation, and the intended use or field of use for the invention generally will not limit the scope of a claim." The Applicants respectfully remind the Examiner that, while this is true for **product** claims, the pending claims are **method** claims, and thus the recitation in claim 43 and its dependent claims of "wherein the method is used to treat anemia associated with a condition selected from the group consisting of ...." defines a patient population (or group of patient populations) on which the method is performed, and thus serves as a limitation. The Examiner's own language in the sentence immediately following that recited above (ie: "where the claimed and prior art **products** are identical or substantially identical...") supports this argument.

In summary, the combination of Mrug et al. and Pfeilschifter et al. would teach one of skill in the art that AII(1-6) does not act via AT1 receptor and teach away from using it to stimulate erythropoiesis in view of Mrug et al. and Pfeilschifter et al. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C.§103(a) be withdrawn.

Double Patenting

6. The Examiner rejected claims 1-2, 31-33, 38 and 40-44 for obviousness-type double patenting as being unpatentable over claims 1-11 of US Patent No. 6,239,109.

The Applicants acknowledge the rejection, and will consider filing a terminal disclaimer once the pending claims are otherwise allowable.

Conclusion

The Applicants believe that the application is now in condition for allowance based on the foregoing remarks and amendments. If there is any problem, the Examiner is respectfully invited to contact the undersigned attorney at (312) 913-2106.

Respectfully submitted,

8/23/02

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APPENDIX A (MARKED CLAIMS FOR 98,009-B1)

1.(Amended) A method for augmenting erythropoiesis comprising contacting erythroid progenitor cells with an amount effective to augment erythropoiesis of at least one active agent comprising a sequence of at least three contiguous amino acids of groups R^1-R^8 in the sequence of general formula I

$$R^1\text{-}R^2\text{-}R^3\text{-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8$$

wherein R^1 is selected from Asp, Glu, Asn, Acpc, Ala, Me^2Gly, Pro, Bet, $Glu(NH_2)$, Gly, $Asp(NH_2)$ and Suc;

R^2 is selected from Arg, Lys, Ala, Orn, Ser(Ac), Sar, D-Arg and D-Lys;

R^3 is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc, Lys and Tyr;

R^4 is selected from the group consisting of Tyr, $Tyr(PO_3)_2$, Thr, Ser, Ala, homoSer and azaTyr;

R^5 is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R^6 is selected from the group consisting of His, Arg or 6-NH_2-Phe;

R^7 is selected from the group consisting of Pro or Ala; and

R^8 is selected from the group consisting of Phe, Phe(Br), Ile and Tyr[,]; excluding sequences including R^4 as a terminal Tyr group, and

wherein the active agent is not SEQ ID NO:1 or SEQ ID NO:19,

for a time and under conditions effective to augment erythropoiesis.

40.(Amended) The method of claim 1 wherein the contacting occurs in vivo and a dosage of active agent is between [~~about~~] 0.1 ng/kg and [~~about~~] 10.0 mg/kg.

41.(Amended) The method of claim 1 wherein the contacting occurs in vitro and a dosage of active agent is between [~~about~~] 0.1 ng/ml and [~~about~~] 10.0 mg/ml.

45. (New) The method of claim 43, wherein the anemia is associated with chronic renal failure.

46.(New) The method of claim 43, wherein the anemia is associated with end-stage renal disease.

47.(New) The method of claim 43, wherein the anemia is associated with renal transplantation.

48. (New) The method of claim 43, wherein the anemia is associated with cancer.

49.(New) The method of claim 43, wherein the anemia is associated with acquired immune deficiency syndrome.

50.(New) The method of claim 43, wherein the anemia is associated with chemotherapy.

51.(New) The method of claim 43, wherein the anemia is associated with radiotherapy.

52.(New) The method of claim 43, wherein the anemia is associated with bone marrow transplantation.